SYNTHETIC COMMUNICATIONS, 29(5), 891-903 (1999)

A CONVENIENT AND PRACTICAL SYNTHESIS OF COENZYME B_{12} ENRICHED IN ^{13}C IN THE COBALT-BOUND CARBON

Shifa Cheng*†, Erle Zang‡, Kenneth L. Brown*‡

†Department of Chemistry, Xavier University of Louisiana, New Orleans, LA 70125. ‡Department of Chemsitry, Ohio University, Athens, OH 45701.

Abstract: [A15-^{13}C]Adenosylcobalamin in which the labeled carbon is bound to the cobalt atom, and its analogs were synthesized from D-[5-^{13}C]ribose through anomeric hydroxyl activation, coupling with adenosines, and then alkylation of reduced B_{12}. The synthetic routes described here are mild, efficient, and proceed in reasonable yield.

Coenzyme B_{12} (5'-deoxyadenosylcobalamin, AdoCbl, Figure) is of considerable interest on many grounds. Enzymes dependent on coenzyme B_{12} are well known to induce a highly efficient cleavage of the carbon-cobalt bond of this organometallic coenzyme.[1-4] The rate of this thermal carbon-cobalt bond homolysis is believed to be enhanced by some 9 to 12 orders of magnitude[5-6] relative to the nonenzymatic thermolysis of AdoCbl. While it is still not clear what mechanism(s) these enzymes use to achieve this tremendous catalysis, it is possible that the hydrogen bonding interactions between the adenosyl ligand and

* To whom correspondence should be addressed.

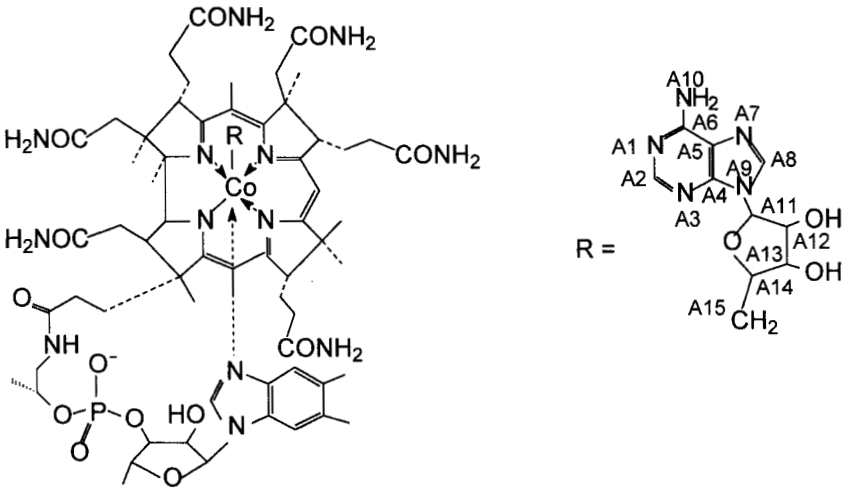


FIGURE: Structure of Coenzyme B_{12} (AdoCbl) and Numbering of 5'-Deoxyadenosyl Group (A15 carbon is linked to Co in B_{12}).

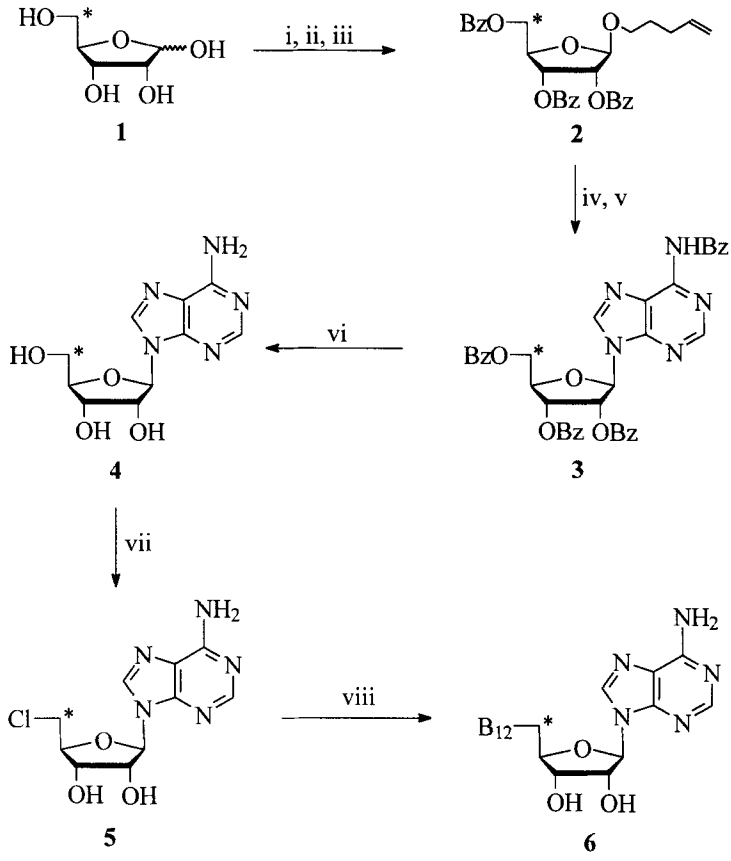
the enzymes play an important role in the enzymatic "activation" of carbon-cobalt bond cleavage. In order to permit NMR studies of the mechanism(s) of this reaction, the synthesis of coenzyme B_{12} labeled with ^{13}C in the cobalt-bound carbon ([A15-^{13}C]AdoCbl) and structural analogs similarly labeled is highly desirable. The synthesis of these cobalamins requires the synthesis of [5'-^{13}C]-adenosine. Such labeled compounds are likely not only to be important in the mechanistic studies of coenzyme B_{12}, but also to be of wide use in coordination chemistry and nucleic acid chemistry.

Only one synthetic route for preparation of [A15-^{13}C]AdoCbl appears to have been reported by Hogenkamp and co-workers.[7] It was synthesized from 90% enriched potassium [^{13}C]cyanide and L-erythrose. This procedure is tedious (11 steps) and the overall chemical yield (< 3% based on labeled cyanide) is very

low. Since D-[5-^{13}C]ribose is now commercially available, the [5-^{13}C]adenosines may now be conveniently synthesized from D-[5-^{13}C]ribose as starting material, activating the anomeric hydroxyl group by formation of the pent-4-enyl riboside, and then coupling with purine bases in the presence of trifluoromethanesulfonic acid and *N*-iodosuccinimide (NIS/TfOH) (Scheme).

In the presence of catalytic amounts of camphorsufonic acid, the Fischer glycosidation of [5-^{13}C]D-ribose with 4-pentenol overnight produced "armed" pent-4-enyl-β-D-*erythro*-pentofuranoside after neutralization with silver carbonate. The overnight reaction time was necessary for the glycosidation reaction to be complete. Without purification, the intermediate was benzoylated with benzoyl chloride in pyridine. The protected [5'-^{13}C]pent-4-enyl-2',3',5'-tri-*O*-benzoyl-β-D-*erythro*-pentofuranoside, **2**, was easily isolated in 88% yield by flash chromatography, and its structure was primarily the β configuration as suggested by Chapeau and Marnett.[8] Compound **2** was stable and could be stored at 5 °C for months without any sign of chemical change. It was then used as a common intermediate for the synthesis of [5'-^{13}C]adenosine and its analogs by coupling with varying purines.

The protected compound **2** was disarmed and coupled with N^6-benzoylaminopurine to produce [5'-^{13}C]N^6,2',3',5'-tetra-*O*-benzoyladenosine (**3**) in the presence of iodonium ion generated *in situ* from *N*-iodosuccinimide (NIS) and trifluoromethanesulfonic acid (TfOH). The protection of exocyclic amino group was necessary to prevent undesired reactions. Dry acetonitrile seemed to be



SCHEME: i) 4-pentenol, CSA, r.t. overnight; ii) $AgCO_3$ (excess); iii) BzCl, pyridine, overnight; iv) N^6-benzoyl aminopurine, TfOH/NIS, CH_3CN; v) 1.0 M K_2HPO_4; vi) NH_3/CH_3OH; vii) SO_2Cl_2, HMPA; viii) cob(II)alamin.

important in the reproducibility of this coupling reaction. The desired β-linkage in the product, **4**, was achieved due to the participation of 2' benzoyl ester in **3**. Without purification, **3** was easily de-*O*- and de-*N*-benzoylated with methanolic ammonium to produce [5'-^{13}C]adenosine (**4**). This procedure was also used for the

synthesis of [5'-^{13}C]N^6-methyladenosine and [5'-^{13}C]N^6,N^6-dimethyladenosine. In the latter two cases, N^6-amino group was protected by the methyl(s).

The conversion of [5'-^{13}C]adenosine to [5'-^{13}C]5'-chloro-5'-deoxyadenosine (**5**) was accomplished using a modification of Kikugawa-Ichino method.[7,9] The chloride was then reacted in the dark with $Co^{(II)}$-cobalamin (cob(II)alamin) which was prepared by reducing deaerated cyanocobalamin in 10% aqueous NH_4Cl with zinc to give [A15-^{13}C]AdoCbl. As expected, the physical properties, including HPLC retention time, UV-vis spectra under various conditions, and 1D/2D ^{1}H and ^{13}C NMR of [A15-^{13}C]AdoCbl, are all identical to those of unlabeled AdoCbl.[7]

Our experiments show that the pentenyl riboside, **2**, which was an extension of Fraser-Reid's pentenyl glycosides[10-12] by Marnett,[8] is a convenient and useful reagent for the synthesis of nucleosides. Although D-ribose exists in an equilibrium between furanose and pyranose forms, we observed only one product in the furanose form. Pentenyl riboside reacts with purine derivatives under mild conditions in the presence of the NIS/TfOH catalyst to afford the adenosine derivatives. The 2-benzoyl group directs the incoming purine to the β face of the ribose in the coupling step. The overall yields are satisfactory based on labeled D-ribose. Thus the synthetic route provides a convenient and practical way to produce ^{13}C labeled adenosylcobalamin and structural analogs thereof.

Experimental:

^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian Unity Inova 400 MHz or 500 MHz spectrometer. All of the reagents except [5-^{13}C]D-ribose

(Cambridge Isotopes) were purchased from Aldrich and used without further purification.

[5'-^{13}C]Pent-4-enyl 2',3',5'-tri-*O*-benzoyl-β-D-*erythro*-pentofuranoside (2)

To a mixture of 15 mL of 4-pentenol and 2 mL of 1% camphorsufonic acid (CSA) in 4-pentenol, 500 mg of [5-^{13}C]D-ribose (**1**) was added. After overnight reaction, excess Ag_2CO_3 was added in the dark to terminate the reaction and the suspension was filtered. The unreacted 4-pentenol was recovered under reduced pressure. After removal of solvent, the residue was dissolved in 10 mL of pyridine and an excess of benzoyl chloride (3 mL, BzCl) was added. The reaction was allowed to proceed overnight. Water (50 mL) was added and the aqueous solution was extracted with ethyl ether (3 x 20 mL). The ether extract was washed with water (50 mL), 5% H_2SO_4 (50 mL), and 1.0 M Na_2CO_3 solution (100 mL), dried over $MgSO_4$, and finally filtered. After removal of the ether by rotary evaporation, the residue was subjected to column chromatography (silica gel 100-200 mesh, hexane-ethyl acetate = 100:3 to 100:10) to give product **2** (1.48 g, 88% yield). ^{1}H NMR ($CDCl_3$) δ: 8.07 (d, 2H, ortho Ph**H**, J = 7.00 Hz), 8.03 (d, 2H, ortho Ph**H**, J = 7.00 Hz), 7.90 (d, 2H, ortho Ph**H**, J = 7.00 Hz), 7.58 - 7.29 (m, 9H, meta and para Ph**H**), 5.89 (dd, 1H, **H3'**), 5.76 (m, 1H, **H4**), 5.70 (d, 1H, **H2'**), 5.25 (s, 1H, **H1'**), 4.98 (m, 2H, **H5**), 4.51 - 4.75 (m, 3H, **H4'** and **H5'**), 3.79 (m, 1H, 1 **H1**), 3.46 (m, 1H, 1 **H1**), 2.09 (q, 2H, **H3**), 1.64 (m, 2H, **H2**). ^{13}C NMR ($CDCl_3$) δ: 166.18, 165.40, 165.30 (3 benzoyl **C**(O)), 137.89 (**C4**), 133.45,

133.35, 133.11, 129.82, 129.80, 129.75, 129.38, 128.09, 128.50, 128.37 (benzoyl **C**'s on benzene ring), 115.01 (**C5**), 105.63 (**C1'**), 78.90 (**C4'**), 75.67 (**C2'**), 72.68 (**C3'**), 67.87 (**C1**), 65.01 (**C5'**), 30.3 (**C3**), 28.59 (**C2**).

General procedure for praparation of [5'-^{13}C]adenosine (4) and its analogs

[5'-^{13}C]Pent-4-enyl-2',3',5'-tri-*O*-benzoyl-β-D-*erythro*-pentofuranoside, **2**, (220 mg, 0.456 mmol) and *N*-iodosuccinimide (NIS, 93 mg, 0.456 mmol) were dried under vaccum overnight. To the mixture, N^6-benzoyl aminopurine (109 mg, 0.456 mmol) and 10 mL of acetonitrile were added. The mixture was stirred for about 10 min. Triflic acid (TfOH, 0.041 mL) was added and the reaction was allowed to proceed for about 5 hrs. The reaction was terminated by adding 1.0 M K_2HPO_4 solution (35 mL). The solution was then extracted with ether (20 mL x 4), the combined ether layers were washed with water (20 mL x 3), dried over Na_2SO_4, and filtered. After removal of ether with a rotary evaporator, the residue (crude product **3**) was added methanolic ammonium solution (60 mL). The solution was stirred about 24 hrs at room temperature. After removal of the solvent with a rotary evaporator, water (40 mL) was added to dissolve the residue. The aqueous solution was then extracted with ether (20 mL x 3), the combined ether layers were washed with water twice, and the aqueous layers were combined with the original aqueous solution. The combined aqueous solution was evaporated to dryness under reduced pressure to give corresponding product. If necessary, further purification was carried out on Dowex 50 X8 column. The

inpure product was dissolved in water, and the aqueous solution was loaded on Dowex 50 X8 column. After washing with copious amount of water, 1.0 M aqueous NH_4OH eluted the product.

[5'-^{13}C]Adenosine 4: 43% yield. ^{1}H NMR (DMSO-d_6) δ: 8.33 (s, 1H, **H8** purine), 8.12 (s, 1H, **H2** purine), 7.34 (s, 2H, N**H**$_2$), 5.86 (d, 1H, **H1'**, J = 6.4 Hz), 5.42 (m, 2H, 2 O**H**), 5.18 (d, 1H, O**H**, J = 4.80 Hz), 4.60 (q, 1H, **H2'**), 4.13 (q, 1H, **H3'**), 3.95 (q, 1H, **H4'**), 3.51 - 3.69 (m, 2H, **H5'**). ^{13}C NMR (DMSO-d_6) δ: 156.1 (C6), 152.3 (C2), 149.0 (C4), 139.8 (C8), 119.3 (C5), 87.8 (C1'), 85.8 (C4'), 73.4 (C2'), 70.6 (C3'), 61.6 (C5').

[5'-^{13}C]N^6-Methyladenosine: 55% yield. ^{1}H NMR (DMSO-d_6) δ: 8.37 (s, 1H, **H8** purine), 8.26 (s, 1H, **H2** purine), 7.85 (s, 1H, N**H**$_2$), 5.91 (d, 1H, **H1'**, J = 6.00 Hz), 5.47 (m, 2H, 2 O**H**), 5.23 (d, 1H, O**H**, J = 4.50 Hz), 4.64 (q, 1H, **H2'**), 4.17 (q, 1H, **H3'**), 4.00 (q, 3H, **H4'**), 3.56 - 3.72 (m, 2H, **H5'**), 2.99 (s, 3H, NC**H**$_3$). ^{13}C NMR (DMSO-d_6) δ: 156.7 (C6), 154.0 (C2), 149.7 (C4), 141.2 (C8), 121.5 (C5), 89.5 (C1'), 87.5 (C4'), 75.1 (C2'), 72.2 (C3'), 63.3 (C5'), 28.6 (NCH_3).

[5'-^{13}C]N^6,N^6-Dimethyladenosine: 48% yield. ^{1}H NMR (DMSO-d_6) δ: 8.40 (s, 1H, **H8** purine), 8.24 (s, 1H, **H2** purine), 5.94 (d, 1H, **H1'**, J = 5.00 Hz), 5.48 (d, 1H, O**H**, J = 6.50 Hz), 5.42 (dd, 1H, 5' O**H**), 5.22 (d, 1H, O**H**, J = 5.00 Hz), 4.61 (q, 1H, **H2'**), 4.17 (q, 1H, **H3'**), 3.99 (q, 1H, **H4'**), 3.56 - 3.72 (m, 2H, **H5'**), 3.40

(s, 6H, $N(CH_3)_2$). ^{13}C NMR (DMSO-d_6) δ: 155.9 (C6), 153.3 (C2), 151.5 (C4), 140.2 (C8), 121.4 (C5), 89.4 (C1'), 87.3 (C4'), 75.1 (C2'), 72.1 (C3'), 63.1 (C5'), 39.5 ($N(CH_3)_2$).

General procedure for preparation of [5'-^{13}C]5'-chloro-5'-deoxyadenosine (5) and its analogs (Examplified with 5)

Dry **[5'-^{13}C]**adenosine, **5**, (100 mg, 0.374 mmol) was dissolved in a mixture of thioyl chloride (0.15 mL) and hexamethylphosporamide (HMPA, 1.0 mL). The reaction was allowed to proceed overnight. Water (50 mL) was then added, the aqueous solution was applied to a Dowex 50 X8 (H^+ form) column. After washing with copious amounts of water, the column was eluted with 500 mL of 1.0 M NH_4OH. Removal of ammonium hydroxide solution with a rotary evaporator gave the product **5** (72 mg, 67% yield). ^1H NMR (DMSO-d_6) δ: 8.33 (s, 1H, **H8** purine), 8.14 (s, 1H, **H2** purine), 7.30 (s, 2H, NH_2), 5.92 (d, 1H, **H1'**, J = 5.60 Hz), 5.63 (d, 1H, O**H**, J = 5.60 Hz), 5.49 (d, 1H, O**H**, J = 4.8 Hz), 4.74 (q, 1H, **H2'**), 4.21 (q, 1H, **H3'**), 4.08 (q, 1H, **H4'**), 3.81 - 3.96 (m, 2H, **H5'**). ^{13}C NMR (DMSO-d_6) δ: 156.0 (C6), 152.6 (C2), 149.4 (C4), 139.6 (C8), 119.1 (C5), 87.4 (C1'), 83.6 (C4'), 72.6 (C2'), 71.2 (C3'), 44.7 (C5').

[5'-^{13}C]5'-Chloro-5'-deoxy-N^6-methyladenosine: 56% yield. ^1H NMR (DMSO-d_6) δ: 8.36 (s, 1H, **H8** purine), 8.28 (s, 1H, **H2** purine), 7.81 (s, 1H, N**H**), 5.97 (d, 1H, **H1'**, J = 6.00 Hz), 5.64 (bs, 1H, O**H**), 5.51 (bs, 1H, O**H**), 4.78 (t, 1H, **H2'**),

4.26 (t, 1H, **H3'**), 4.12 (m, 3H, **H4'**), 3.85 - 4.00 (m, 2H, **H5'**), 2.98 (s, 3H, NCH_3). ^{13}C NMR (DMSO-d_6) δ: 156.7 (C6), 154.3 (C2), 150.2 (C4), 141.0 (C8), 121.2 (C5), 89.1(C1'), 85.2 (C4'), 74.3 (C2'), 72.8 (C3'), 46.4 (C5'), 28.6 (NCH_3).

[5'-^{13}C]5'-Chloro-5'-deoxy-N^6,N^6-dimethyladenosine: 46% yield. ^1H NMR (DMSO-d_6) δ: 8.38 (s, 1H, **H8** purine), 8.26 (s, 1H, **H2** purine), 5.99 (d, 1H, **H1'**, J = 5.20 Hz), 5.66 (bs, 1H, O**H**), 5.53 (bs, 1H, O**H**), 4.74 (t, 1H, **H2'**), 4.25 (m, 1H, **H3'**), 4.12 (m, 1H, **H4'**), 3.84 - 4.00 (m, 2H, **H5'**), 3.42 (s, 6H, $N(CH_3)_2$). ^{13}C NMR (DMSO-d_6) δ: 155.9 (C6), 153.6 (C2), 151.9 (C4), 139.9 (C8), 121.2 (C5), 89.0 (C1'), 85.1 (C4'), 74.4 (C2'), 72.8 (C3'), 46.4 (C5'), 38.0 ($N(CH_3)_2$).

General procedure for preparation of [A15-^{13}C]AdoCbl (6) and its analogs

Cyanocobalamin (CNCbl, 100 - 200 mg, excess reagent) was dissolved in 150 mL of 10% NH_4Cl solution, and deaerated by bubbling argon or N_2 for 60 min. Excess Zn wool (freshened by treating with 1.0 M HCl for 5 min and washing well with water) was added. After reduction for 90 - 120 min to completely convert CNCbl to cob(II)alamin, a deaerated solution of the nucleoside chloride (**5** or its analogs) was transferred by canula into the solution to initiate the alkylation. The reaction was allowed to proceed overnight. The reaction solution was poured into 1.0 M HCl solution (20 mL), and the acidic solution was then desalted on an Amberlite XAD-2 column.[13] After washing with water to remove most of the aquacobalamin (H_2OCbl), the red band was eluted with 50% acetonitrile water mixture. The eluent was directly applied onto SP-

Sephadex (Sigma, 40-120μ) cation exchange column. Water elution gave the product **6** (or its analogs) in quantitative yield based on the nucleoside chloride. UV spectra were the same as those of unlabeled AdoCbl and were identical to those reported in literature.[7] Purity: >98% by HPLC (Beckmann C18 reversed phase column, isocratic at 5% CH_3CN/95% pH3 phosphate buffer for 1 min, gradient increase to 30% CH_3CN/70% pH3 phosphate buffer in 8 min, gradient decrease back to 5% CH_3CN/95% pH3 phosphate buffer at 13 min. 2 mL/min.) for all products with retention times at 7.7 min for [A15-^{13}C]AdoCbl, 6.7 min for N^6-methyl-[A15-^{13}C]AdoCbl, and 7.2 min for N^6,N^6-dimethyl-[A15-^{13}C]AdoCbl.

[A15-^{13}C]AdoCbl: ^{1}H NMR (D_2O, downfield region only) δ: 8.19 (s, 1H), 8.00 (s, 1H), 7.16 (s, 1H), 6.95 (s, 1H), 6.26 (s, 1H), 6.24 (s, 1H), 5.93 (s, 1H), 5.56 (s, 1H). ^{13}C NMR (D_2O) δ: 180.77, 180.71, 179.94, 178.98, 178.68, 178.44, 178.40, 177.86, 177.59, 177.28, 172.78, 166.82, 166.23, 158.28, 155.56, 151.46, 144.28, 143.43, 140.64, 136.40, 134.13, 133.03, 121.51, 121.05, 113.14, 108.14, 106.70, 97.39, 90.57, 88.99, 88.19, 88.05, 84.15 (d, J_{PC} = 8.92 Hz), 76.40, 76.11, 75.78 (d, J_{PC} = 4.16 Hz), 75.58 (J_{PC} = 6.28 Hz), 75.14, 71.69, 62.96, 60.50, 58.13, 57.06, 55.44, 52.77, 49.10, 49.05, 47.39, 45.82, 44.94, 42.27, 37.89, 37.76, 34.45, 34.35, 34.17, 33.84, 29.98, 28.98, 28.43, 27.45 (**A15**), 23.59, 23.23, 22.22, 21.93, 21.41, 21.35, 19.52, 19.28, 18.46, 17.99.

***N*^{6}-methyl-[A15-^{13}C]AdoCbl**: ^{1}H NMR (D_2O, downfield region only) δ:[14] 8.20 (s, 1H), 7.97 (s, 1H), 7.20 (s, 1H), 7.01 (s, 1H), 6.31-6.29 (d, 2H), 5.97 (s, 1H),

5.59 (s, 1H). ^{13}C NMR (D_2O) δ: 180.73, 180.59, 179.88, 178.94, 178.63, 178.32, 178.31, 177.81, 177.55, 177.20, 172.69, 166.69, 166.14, 157.63, 155.44, 150.12, 144.24, 142.57, 140.65, 136.21, 133.93, 132.98, 121.75, 120.95, 113.06, 108.07, 106.61, 97.25, 90.48, 88.89, 88.11, 87.96, 84.09 (d, J_{PC} = 8.42 Hz), 76.33, 76.18, 75.73 (d, J_{PC} = 3.14 Hz), 75.48 (d, J_{PC} = 6.16 Hz), 75.19, 71.70, 62.98, 60.43, 58.03, 56.97, 55.33, 52.63, 48.99, 48.92, 47.47, 45.75, 44.95, 42.16, 38.46, 37.85, 37.71, 34.49, 34.43, 34.33, 34.21, 33.71, 29.84, 28.86, 28.38, 26.83 (**A15**), 23.60, 23.19, 22.19, 21.91, 21.38 (d, J_{PC} = 4.53 Hz), 21.30, 19.44, 19.22, 18.41, 17.94.

***N*^{6},*N*^{6}-dimethyl-[A15-^{13}C]AdoCbl**: ^{1}H NMR (D_2O, downfield region only) δ: 8.14 (s, 1H), 7.94 (s, 1H), 7.22 (s, 1H), 7.03 (s, 1H), 6.35-6.33 (d, 2H), 5.99 (s, 1H), 5.62 (s, 1H). ^{13}C NMR (D_2O) δ: 180.68, 180.53, 179.85, 178.92, 178.58, 178.29, 178.28, 177.78, 177.51, 177.17, 172.67, 166.65, 166.12, 156.76, 154.76, 151.68, 144.24, 141.09, 140.64, 136.16, 133.90, 132.97, 121.68, 120.92, 113.06, 108.05, 106.62, 97.24, 90.19, 88.86, 87.95, 87.94, 84.10 (d, J_{PC} = 8.42 Hz), 76.32, 76.22, 75.71 (d, J_{PC} = 4.60 Hz), 75.45 (d, J_{PC} = 5.41 Hz), 75.25, 71.70, 62.98, 60.43, 58.02, 56.98, 55.30, 52.60, 48.98, 48.87, 47.46, 45.72, 45.00, 42.13, 41.44, 38.44 (d, J_{PC} = 4.53 Hz), 37.84, 37.68, 34.48, 34.44, 34.33, 34.22, 33.71, 29.82, 28.83, 28.38, 26.81 (**A15**), 23.58, 23.21, 22.18, 21.90, 21.38 (d, J_{PC} = 4.53 Hz), 21.30, 19.40, 19.22, 18.40, 17.94.

Acknowledgment. This research was supported by the National Institute of General Medical Sciences, Grant GM 48858 (to K.L.B.).

References

1. Valinsky, J. E.; Abeles, R. H.; Mildvan, A. S. *J. Biol. Chem.* **1974**, *249*, 2751.
2. Valinsky, J. E.; Abeles, R. H.; Fee, J. A. *J. Am. Chem. Soc.* **1974**, *96*, 4709.
3. Hollaway, M. R.; White, H. A.; Joblin, K. N.; Johnson, A. W.; Lappert, M. F.; Wallis, O. C. *European J. Biochem.* **1978**, *82*, 143.
4. Babior, B. M.; Moss, J. H.; Gould, D. C. *J. Biol. Chem.* **1972**, *247*, 4389.
5. Hay, B. P.; Finke, R. G. *J. Am. Chem. Soc.* **1986**, *108*, 4820.
6. Brown, K. L.; Cheng, S.; Marques, H. M. *Inorg. Chem.* **1995**, *34*, 3038.
7. Walker, T. E.; Hogenkamp, H. P. C.; Needham, T. E.; Matwiyoff, N. A. *Biochemistry* **1974**, *13*, 2650.
8. Chapeau, M.-C.; Marnett, L. J. *J. Org. Chem.* **1993**, *58*, 7258.
9. Kikugawa, K.; Ichino, M. *Tetrahedr. Lett.* **1971**, *2*, 87.
10. Fraser-Reid, B.; Udodong, U. E.; Wu, Z.; Ottosson, H.; Merritt, J. R.; Rao, C. S.; Roberts, C.; Madsen, S. *Synlett* **1992**, *12*, 927.
11. Fraser-Reid, B.; Konradsson, P.; Mootoo, D. R.; Udodong, U. *J. Chem. Soc., Chem. Commun.* **1988**, 823.
12. Mootoo, D. R.; Date, V.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1988**, *110*, 2662.
13. Brown, K. L.; Hakimi, J. M.; Nuss, D. M.; Montejuno, Y. D.; Jacobsen, D. W. *Inorg. Chem.* **1984**, *23*, 1463.
14. Fleming, P. E.; Daikh, B. E.; Finke, R. G. *J. Inorg. Biochem.* **1998**, *69*, 45.

(Received in the USA 08 September 1998)